

**REMARKS**

The application is considered to contain 108 groups of inventions (Groups 1-108) which are not so linked as to form a single general inventive concept under PCT Rule 13.1. The examiner holds that under PCT Rule 13.2, Groups 1-108 lack the same or corresponding special technical features because JP7-285997 is said to teach an agonist to TNF-R1, the mutein having a substitution at position 86 from the N-terminus of the amino acid sequence set forth in SEQ ID NO:1.

Applicants elect with traverse Group 13 (SEQ ID NO:21; clone 37 shown in Table 2 at page 24 of the present specification), drawn to a TNF antagonist comprising the amino acid sequence of SEQ ID NO:21 and presently comprising claims 1-4, 6 and 8-9.

Traversal is based on the fact that JP7-285997 does not disclose a tumor necrosis factor mutant protein where four or more amino acid residues selected from the group consisting of residues 29, 31, 32, 84-89, 145, 146 and 147 of SEQ ID NO:1 are replaced. The only mutant proteins disclosed in JP7-285997 are those where:

(1) the 86th amino acid residue is replaced by threonine,

(2) the 86th and 29th amino acid residues are replaced by threonine and serine, respectively,

(3) the 86th and 31st amino acid residues are replaced by threonine and glutamic acid, respectively,

(4) the 86th and 32nd amino acid residues are replaced by threonine and tryptophan acid, respectively,

(5) the 86th, 29th and 32nd amino acid residues are replaced by threonine, serine and tryptophan acid, respectively, and

(6) the 86th, 31st and 32nd amino acid residues are replaced by threonine, asparagine and tryptophan acid, respectively.

Clearly, the mutant proteins of JP'997 only have one, two or three amino acid substitutions and cannot defeat the special technical feature shared by the presently amended claims.

Reconsideration and withdrawal of the restriction requirement are therefore respectfully requested.

The amendment to claim 10 is made merely to correct a typographical error, and the amendment to claim 1 to recite that "four or more" amino acid residues selected from residues 29, 31, 32, 84-89, 145, 146, and 147 of SEQ ID NO:1 are replaced with other amino acids is supported by the present specification in Tables 1 and 2 at pages 23-24, where clones 4-9 in Table 1 and all clones 15-38 in Table 2 have "four or more" amino acid residues of residues 29, 31, 32, 84-89, 145, 146 and 147 replaced

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with other amino acid residues. No new matter is being added by this amendment.

Furthermore, because the examiner has required restriction between product and process claims and, as applicants have elected claims directed to a product, it is also understood that if product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim(s) will be considered for rejoinder.

Favorable consideration and early allowance are respectfully solicited.

Respectfully submitted,

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